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NOTICE OF ALLOWANCE AND FEE(S) DUE

23552 7590 10/18/2010

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
BRADLEY, CHRISTINA	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/18/2010

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,439	01/05/2007	Bruno Lussier	09555.0151USWO	4659

TITLE OF INVENTION: USE OF GROWTH HORMONE RELEASING FACTOR ANALOGS IN TREATING PATIENTS SUFFERING FROM WASTING

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$755	$300	$0	$1055	01/18/2011

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

23552 7590 10/18/2010

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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nonprovisional	YES	$755	$300	$0	$1055	01/18/2011

EXAMINER	ART UNIT	CLASS-SUBCLASS
BRADLEY, CHRISTINA	1654	514-011200

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 336 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 336 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/576,439	LUSSIER ET AL.	
	Examiner	Art Unit	
	CHRISTINA BRADLEY	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 10/08/2010*.

2. ☒ The allowed claim(s) is/are *3,8-14,16 and 22-24*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Christina Marchetti Bradley/
Primary Examiner, Art Unit 1654

REASONS FOR ALLOWANCE

1. The following is an examiner's statement of reasons for allowance: The closest prior art of Schwartz et al. (US 6,423,693) teach that growth hormone releasing hormone (GHRH or GRF) has therapeutic utility in stimulating the production and secretion of growth hormone (GH) (col 2, lines 30-37) and specifically in the treatment of cachexia in chronic diseases such as cancer (col 2, lines 38-48, col 34, line 44 - col 35, line 18) and the treatment of chronic obstructive pulmonary disorder (col 11, lines 55-65). Schwartz et al. teach that current limitations of recombinant GHRH therapy include the short half-life of the peptides *in vivo* and the requirement for frequent administration (1-3 times/day) of either subcutaneous or intravenous injections (col 2, lines 49-57). Schwartz et al. propose a gene-therapy approach to deliver GHRH to wasting patients in order to circumvent the limitations of rGHRH administration. The reference neither teaches nor discloses the administration of the GRF analog SEQ ID NO: 7 to patients suffering from wasting.

2. Larocque et al. ("Anchoring rigid hydrophobic chains to stabilize growth hormone-releasing factor," APS Poster, 2001) teach a composition the GRF analog (trans3 hexenoyl) hGRF(1-44)NH_2 (instant SEQ ID NO: 7, Figure 1, Figures 3A and B). Larocque et al. teach that this analog has a prolonged half life in human serum which translates into a higher GH-releasing potency in pigs, inducing GH release on a 8-hour period in a pulsatile fashion following sc administration at low doses (0.11 to 3 mg/kg). Larocque et al. teach that this analog is therefore a powerful and long-acting GH secretagogue with all the physiological advantages of hGRF and is in clinical development for the stimulation of anabolism in several age-related diseases and conditions, such as recovery following hip fracture, COPD and frail elderly.

3. Applicants have demonstrated unexpected results which are sufficient to render the claims patentable over Schwartz et al. and Larocque et al.

4. As stated by Applicant on pp. 12-13 of the response filed 05/04/2010, the prior art of Schwartz et al. and Larocque et al. does not address the effect of GHRH on muscle function in a patient suffering from severe wasting. Schwartz et al. reasons that based on the known effects of growth hormone on muscle mass, GHRH, which stimulates growth hormone, could be used to treat wasting. On p. 13-14 of the response filed 05/04/2010, Applicants present evidence that an increase in muscle mass following growth hormone administration does not correlate with an increase in muscle function (see Zachwieja & Yarasheski, Lissett & Shalet, Burdet et al. and Pape et al. Appendix A-D filed 05/04/2010). In contrast, the inventors have shown in a randomized, double-blind, placebo-controlled study, that administration of SEQ ID NO: 7 to subjects with stable COPD increases muscle mass and muscle function (see Example 6 of the original specification, especially Table 2 which shows that the Low BMI (BMI <20) and Low FFMI groups (FFMI <16 for men and <15 for women), which suffer from severe wasting according to the characteristics in the instant claims, exhibit an increase in muscle function in response to SEQ ID NO: 7 as compared to placebo). The effect of SEQ ID NO: 7 on muscle function in patients suffering from severe wasting could not have been predicted from Schwartz et al. and Larocque et al., as evidenced by Zachwieja & Yarasheski, Lissett & Shalet, Burdet et al. and Pape et al. Furthermore, it is clear from the prior art of Burdet et al. that an increase in muscle function is a desired clinical outcome for wasting patients and a goal for research in this field (see p. 1800).

5. MPEP § 716.02(c) states: "Evidence of unexpected results must be weighed against evidence supporting *prima facie* obviousness in making a final determination of the obviousness of the claimed invention. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (Claims directed to a method of effecting analgesia without producing physical dependence by administering the levo isomer of a compound having a certain chemical structure were rejected as obvious over the prior art. Evidence that the compound was unexpectedly nonaddictive was sufficient to overcome the obviousness rejection. Although the compound also had the expected result of potent analgesia, there was evidence of record showing that the goal of research in this area was to produce an analgesic compound which was nonaddictive, enhancing the evidentiary value of the showing of nonaddictiveness as an indicia of nonobviousness.)." The facts of the instant case are similar to the facts of *In re May*. Although SEQ ID NO: 7 has the expected result of increasing muscle mass in severe wasting patients, it also has the unexpected result of increasing muscle function in severe wasting patients. Furthermore, there is evidence of record in both in the instant specification and in Burdet et al. showing that the goal of research in this area was to increase muscle function in wasting patients. The unexpected ability to increase muscle function in severe wasting patients outweighs the *prima facie* case for obviousness because the need to increase muscle function in wasting patients is established in the prior art, giving weight and importance to the unexpected discovery of this effect.

6. Finally, the teaching in Larocque et al. that the GRF analog SEQ ID NO: 7 is being used to stimulate anabolism in COPD patients does not anticipate the instant claims because a COPD patient does not necessarily suffer from severe wasting with characteristics a-d of claim 3 (see

Debigare et al. "Peripheral Muscle Wasting in Chronic Obstructive Pulmonary Disease," Am. J. Respir. Crit. Care Med., Volume 164, Number 9, November 2001, 1712-1717) and Larocque et al. nowhere teach administering SEQ ID NO: 7 to severe wasting patients with characteristics a-d of claim 3.

7. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINA BRADLEY whose telephone number is (571)272-9044. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 8:30 A.M. to 4:30 P.M.

9. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christina Marchetti Bradley/
Primary Examiner, Art Unit 1654

cmb